PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 09549	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP 03/07317	International filing date *(day/month/year)* 10.06.2003	Priority date *(day/month/year)* 14.06.2002
International Patent Classification (IPC) or both national classification and IPC C07D473/00		
Applicant SUMIKA FINE CHEMICALS CO., LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18.11.2003	13.08.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Goss, I Telephone No. +49 89 2399-8292

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP 03/07317

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-53 as originally filed

Claims, Numbers

1-23 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-23
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-23
Industrial applicability (IA)	Yes:	Claims	1-23
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: EP-A-0 488 336

D2: ADAH S A ET AL: 'Triflic Enolates In the Palladium-Mediated Synthesis of Complex Ethynyl Adenosines' TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 36, no. 36, 4 September 1995 (1995-09-04), pages 6371-6372, XP004027233

D3: NAIR V ET AL: 'STRATEGICALLY FUNCTIONALIZED ADENOSINES: AGONISTS FOR ADENOSINE RECEPTORS' NUCLEOSIDES & NUCLEOTIDES, MARCEL DEKKER, INC, US, vol. 14, no. 3-5, 1995, pages 537-539, XP009017441

D4: HOCEK M ET AL: 'COVALENT ANALOGUES OF DNA BASE-PAIRS AND TRIPLETS. PART 2: SYNTHESIS AND CYTOSTATIC ACTIVITY OF BIS(PURIN-6-YL)ACETYLENES, -DIACETYLENES AND RELATED COMPOUNDS' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 12, no. 7, 2002, pages 1055-1058, XP009017440

D5: HOCEK M ET AL: 'COVALENT ANALOGUES OF DNA BASE-PAIRS AND TRIPLETS V+. SYNTHESIS OF PURINE-PURINE AND PURINE-PYRIMIDINE CONJUGATES CONNECTED BY DIVERSE TYPES OF ACYCLIC CARBON LINKAGES' COLLECTION OF CZECHOSLOVAK CHEMICAL COMMUNICATIONS, ACADEMIC PRESS, LONDON, GB, vol. 67, no. 10, 2002, pages 1560-1578, XP009017464

D6: MAGER P P: 'NEURAL NETWORK APPROACHES APPLIED TO SELECTIVE A2A ADENOSINE RECEPTOR AGONISTS' MEDICINAL CHEMISTRY RESEARCH, BIRKHAEUSER, BOSTON, US, vol. 8, no. 6, 1998, pages 277-290, XP000952528

D7: LEGRAVEREND M ET AL: 'Synthesis of C2 alkynylated purines, a new family of potent inhibitors of cyclin-dependent kinases' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 8, no. 7, 7 April 1998 (1998-04-07), pages 793-798, XP004136967

D8: CAMAIONI E ET AL: 'NEW SUBSTITUTED 9-ALKYLPURINES AS ADENOSINE RECEPTOR LIGANDS' BIOORGANIC & MEDICINAL CHEMISTRY, ELSEVIER SCIENCE LTD, GB, vol. 6, no. 5, 1998, pages 523-533, XP002926121

D9: MATSUDA A ET AL: 'Nucleosides and nucleotides. 103. 2-Alkyladenosines: a novel class of selective adenosine A2 receptor agonists with potent antihypertensive effects' JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 35, 1992, pages 241-252, XP002170995

D10: BAKKESTUEN A K ET AL: '9-Benzylpurines with inhibitory activity against Mycobacterium tuberculosis' BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 10, no. 11, June 2000 (2000-06), pages 1207-1210, XP004200557

D11: EP-A-1 054 012

1. Novelty

The subject-matter independently claimed in claims 1 and 5 for compounds of general formula I-1 as well as I-2 is not novel in view of the many novelty destroying documents cited in the search report. In this respect the applicant's attention is drawn to each single compound, example or figure as quoted in the search report wherein 2-, 6-, or 8-alkynylpurines have been described. Also the meaning of Z^1 and Z^2 (present nomenclature) being a sugar group, for example pentoses, attached at the 7- or 9-position of the purine nucleus is already known from the prior art.
No further characterising structural element could have been identified.

By restoring novelty (if possible), the novelty rendering feature vis-à-vis the many compounds known from the prior art and also active in the same technical field, has to be clearly indicated.

2. Inventive step

As long as novelty cannot be recognized, a final opinion on inventive step cannot be given. As already anticipated under item 1., by restoring novelty, attention must be paid to define the technical contribution to the already many compounds known from the state of the art, all showing the same pharmacological profile (the aspect of unity of the invention must be carefully considered).

Therefore taking into account **the whole prior art available** an obviousness objection has to be raised, since the skilled person would have tried to provide further compounds expecting them to have the same qualitative activity as those known from D1 to D10.

Consequently, at present it is not possible to first recognize

a) whereon exactly an inventive step could be based, bearing in mind that the problem must have been to provide better compounds (i.e. with improved or unexpected properties) than those already known from the prior art.

b) Further, the problem must be solved by all the compounds claimed re those of the relevant prior art.